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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,324	03/24/2006	Yasuhiko Shiina	P29546	4957

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EXAMINER	
OGUNBIYI, OLUWATOSIN A	
ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
08/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/573,324	SHIINA ET AL.	
	Examiner	Art Unit	
	OLUWATOSIN OGUNBIYI	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/26/06,7/24/06,5/8/09(two) and 6/17/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-14 are pending in the application. Claims 1-10 are under examination

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application (Japan 2003-336438) filed in Japan on 9/26/2003.

Drawings

The drawings in this application have been accepted. No further action by Applicant is required.

Information Disclosure Statement

The information disclosure statements filed 6/26/06 and 5/8/09 has been considered. Initialed copies are enclosed.

The supplemental information disclosure statements filed 7/24/06, 5/8/09 and 6/17/09 fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the supplemental disclosure statement does not include a column that provides a space, next to each document to be considered, for the examiner 's initials. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement,

including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-10 in Paper No. 20081004 is acknowledged. The traversal is on the ground(s) that:

Applicants respectfully submit that the Restriction Requirement fails to satisfy the requirements for supporting a restriction requirement under the PCT Rules. PCT Rules 13.1 and 13.2 state that an international application must relate to one invention only or, if there is more than one invention, those inventions must be so linked as to form a single general inventive concept (Rule 13.1). Inventions are considered linked so as to form a single general inventive concept only when there is a technical relationship involving one or more of the same or corresponding "special technical features." The expression "special technical features" means those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art (Rule 13.2).

Applicants note that this application is an application filed under 35 U.S.C. § 371 and that unity of invention requirements apply. The Examiner's attention is respectfully directed to MPEP 1850 and 37 CFR § 1.475, which explicitly sets forth that "[a]n international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn [] to...[a] process and an apparatus or means specifically designed for carrying out the said process.

" The claims of the present application involve a method for detecting or differentiating rheumatoid arthritis and an antibody specifically recognizing human L-PGDS for using the claimed method. Applicants submit that the restriction requirement is deficient because it does not refer to 37 C.F.R. § 1.475.

Additionally, Applicants respectfully note that the sole basis for the restriction requirement is the Office's reliance on EP 09994471 A1 to Oda et al., which the Office asserts shows that the common feature between the Groups is disclosed in the prior art. Applicants further respectfully remind the Office that, because Oda et al. is the sole basis for the Office's conclusion that a lack of unity exists, the Office will be required to withdraw its conclusion of lack of unity and examine all pending claims upon a conclusion the Oda et al. does not disclose the claimed invention or is not available as prior art. In this regard, Applicants expressly reserve the right to rebut any art-based rejections made on the basis of Oda et al., if such rejections are made.

Applicants' arguments are carefully considered but this is not found persuasive. It is noted that restriction under 35 U.S.C. 121 and 371 is made *a priori* before examination of the claims. As rightly pointed out by Applicants, under PCT Rule 13.1 and 13.2 inventions are considered linked so as to form a single general inventive concept only when there is a technical relationship involving one or more of the same or corresponding "special technical features." PCT Rule 13.2 further states that " The expression "special technical features" means those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art." The technical feature of Group I is a method of detecting or differentiating rheumatoid arthritis including the stage of disease with regard to rheumatoid arthritis and including determining the degree of dysfunction with regard to rheumatoid arthritis comprising measuring the levels of human L-PGDS in a sample. The technical feature of Group II is an antibody that recognizes human L-PGDS. Group II claims are written in product by process format but the claims are drawn to said antibody and not to the methods of using said antibody. Group I and Group II are linked via the technical feature of an antibody that recognizes human L-PGDS. Although, both Group I and Group II require the technical feature of an antibody that recognizes human L-PGDS, this is not a "special technical feature" because the technical feature does not make a contribution over the prior art. As set forth in the restriction requirement, Oda et al (EP 09994471 A1, May 2000, cited in IDS) teaches an antibody specifically recognizing human L-PGDS (see paragraph 10 p.3). For this reason, Group I lacks unity with Group II.

Even though, to 37 C.F.R. § 1.475, sets forth that "[a]n international or a national stage application containing claims to different categories of

invention will be considered to have unity of invention if the claims are drawn [] to...[a] process and an apparatus or means specifically designed for carrying out the said process, the same rule states in part (a) that "An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art."

In the instant case, the technical feature linking the two different categories of invention does not does not make a contribution over the prior art as set forth above.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 20081004.

Claim Objections

Claims 1-7 are objected to because of the following informalities: The claims contains the acronym L-PGDS. Although acronyms are acceptable shorthand in the claims, the first recitation in the claims should be followed by the full meaning. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of detecting or differentiating rheumatoid arthritis, a method of determining the stage of disease with regard to rheumatoid arthritis and determining the degree of dysfunction with regard to rheumatoid arthritis wherein the levels of human L-PGDS in a sample collected from a subject without renal or heart disease or other diseases known to affect the levels of L-PGDS is measured, wherein the levels of human L-PGDS measured is compared to the levels of human L-PGDS in a patient known to have rheumatoid arthritis, does not reasonably provide enablement for the instant methods of detecting or differentiating rheumatoid arthritis, a method of determining the stage of disease with regard to rheumatoid arthritis and determining the degree of dysfunction with regard to rheumatoid arthritis as claimed.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 1 and dependent claims are drawn to a method of detecting or differentiating rheumatoid arthritis, wherein the levels of human L-PGDS in a sample collected from a subject is measured.

Claim 3 and dependent claims are drawn to a method of determining the stage of disease with regard to rheumatoid arthritis, wherein the levels of human L-PGDS in a sample collected from a subject is measured and the stage of disease with regard to rheumatoid arthritis is estimated based on the measurement value.

Claim 5 and dependent claims are drawn to a method of determining the degree of dysfunction with regard to rheumatoid arthritis, wherein the levels of human L-PGDS in a sample is measured and the degree of dysfunction (severity) with regard to rheumatoid arthritis is estimated based on the measurement value.

The facts that should be considered in determining whether a specification is enabling or if it would require an undue amount of experimentation to practice the invention include 1) the quantity of experimentation necessary to make or use the invention based on the content of the disclosure, (2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988). The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. While the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP §

2164.01(a) and the evidence as a whole, the factors that weigh more in making the instant enablement rejection are discussed below.

Nature of the Invention and Breadth of the claims

The claims require the detection of human L-PDGS (lipocalin type prostaglandin synthase) in any type of sample collected from any subject so as to detect or differentiate rheumatoid arthritis, determine the stage of disease or degree of dysfunction with regards to rheumatoid arthritis. The claims do not specify that the subject have rheumatoid arthritis, thus the scope covers detection of LPDGS in both healthy subjects or subjects who have other diseases. The claims do not specify which levels of human L-PDGS i.e. high or low are sufficient for detecting or differentiating rheumatoid arthritis, determining the stage of disease or degree of dysfunction with regards to rheumatoid arthritis, and thus the scope of the claims cover both high and low levels of human L-PDGS in any sample obtained from any type of subject.

The amount of direction or guidance presented and the presence or absence of working examples

The specification teaches that the concentrations of L-PGDS in the blood of rheumatoid arthritis patients are higher than those of healthy volunteers and that the L-PGDS in the blood of rheumatoid arthritis patients tend to increase as the disease progresses and the more the severity of the disease. See fig.1-3

The state of the prior art, predictability or unpredictability in the art

It has been reported that L-PGDS is detected in the blood of an advanced renal disease patient at a high concentration and that L-PGDS concentration in body fluid increases as a result of the production of L-PGDS in atherosclerotic plaque in patients

with ischemic heart disease. See specification p. 4 last bridging paragraph to p. 5 first paragraph. Thus, a high amount of L-PGDS in blood or body fluids is a predictor of diseases such as renal and heart disease other than rheumatoid arthritis. Thus, detection of, for example, high levels of L-PGDS in a sample collected from subjects e.g. with renal or heart disease or subjects without rheumatoid arthritis may not detect or diagnose arthritis or stage of disease or degree of dysfunction but maybe indicative of renal disease or heart disease or other disease in which L-PGDS is a factor. This is also the case for when measurement values of L-PGDS in said subjects are compared with values of L-PGDS in samples collected from healthy volunteers and/or patients with joint diseases other than rheumatoid arthritis. Comparison of L-PGDS levels to those of patients with rheumatoid arthritis who do not have confounding diseases such as renal disease and/or heart disease or other diseases in which L-PGDS levels are elevated is a better indicator of whether a subject has rheumatoid arthritis. Furthermore, ruling out renal disease and heart disease in said subject is also important as L-PGDS levels are elevated in renal disease and heart disease. In addition, a high level of L-PGDS in a subject compared to healthy patients is not necessarily a predictor of rheumatoid arthritis but could be of other diseases such as renal or heart diseases or other diseases in which levels of L-PGDS are elevated. The methods as claimed do not account for all these confounding factors in the diagnosis of rheumatoid arthritis.

Thus, taken together as a whole, one of ordinary skill in the art could conclude that a high level of L-PGDS in a subject is a diagnosis of rheumatoid arthritis when the levels of L-PGDS is compared to the levels of L-PGDS in patients known to have rheumatoid arthritis but not renal disease and heart disease or other diseases in which

levels of L-PGDS are elevated wherein said subject does not have renal or heart disease or other diseases in which levels of L-PGDS are elevated. While, the specification is enabling for a method of detecting or differentiating rheumatoid arthritis, the method of determining the stage of disease with regards to rheumatoid arthritis and determining the degree of dysfunction with regard to rheumatoid arthritis wherein the levels of human L-PGDS in a sample collected from a subject is measured, wherein the levels of human L-PGDS measured is compared to the levels of human L-PGDS in a patient known to have rheumatoid arthritis wherein said subject and patient do not have renal disease and heart disease or other diseases known to affect the levels of L-PGDS, the specification is not enabling for the full scope of the claims as claimed as set forth above.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite because it is not clear how the measurement of levels of human L-PGDS detects or differentiate rheumatoid arthritis, determine the degree of dysfunction and determine the stage of disease. There is no method step tying the measurement of L-PGDS to the preamble of the claim i.e. detecting or differentiating rheumatoid arthritis or determining the degree of dysfunction or determining the stage of disease. For example, do high or low levels of L-PGDS detect or differentiate rheumatoid

arthritis and is there a basis of comparison e.g. to levels of L-PGDS in patients known to have rheumatoid arthritis? The same issue applies to claims 3 and 5.

As to claims 2, 4 and 6, the basis of comparison with a cut-off value that has been predetermined based on classification of measurement values of human L-PGDS in samples collected from healthy volunteers and/or patients with joint diseases other than rheumatoid arthritis (claim 2) or a cut-off value that has been predetermined based on classification of measurement values of human L-PGDS in samples collected from rheumatoid arthritis patients in accordance with stage of disease or degree of dysfunction (claims 4 and 6) is vague and indefinite. The specification does not specially provide a definition for these predetermined cut-off values and the claims do not set forth the above predetermined cut-off value and thus the values being referred to in the claims is not clear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-10 are rejected under 35 U.S.C. 102(a) as being anticipated by Guild et al W) 2003/060465 published July 24, 2003.

Claim 1 and dependent claims are drawn to a method of detecting or differentiating rheumatoid arthritis, wherein the levels of human L-PGDS in a sample collected from a subject is measured.

Claim 3 and dependent claims are drawn to a method of determining the stage of disease with regard to rheumatoid arthritis, wherein the levels of human L-PGDS in a sample collected from a subject is measured and the stage of disease with regard to rheumatoid arthritis is estimated based on the measurement value.

Claim 5 and dependent claims are drawn to a method of determining the degree of dysfunction with regard to rheumatoid arthritis, wherein the levels of human L-PGDS in a sample is measured and the degree of dysfunction (severity) with regard to rheumatoid arthritis is estimated based on the measurement value.

As to claims 2, 4 and 6, the pre-determined cut-off values are not clearly set forth in the claims and therefore the cut-off values are interpreted as levels of human L-PGDS in samples of healthy patients or in RA patients at different stage of disease or severity of disease.

Guild et al teaches a method of detecting rheumatoid arthritis (RA) wherein the levels of human L-PGDS in samples collected from a subject is measured. See abstract, p. 13 lines 17-21, p. 14 lines 6-22, p. 93 and table 1 and 2 p. 108 and p. 140 respectively, marker M177. Said samples include body fluids such as blood fluids, urine, synovial/joint fluid etc. See p. 4 lines 10-16. Said level of L-PGDS is measured by immunoassay. See p. 16 lines 32-34 and p. 16 lines 6-13. Guild et al also teaches

determining the stage of rheumatoid arthritis ("late disease" versus "early disease") by comparing levels of L-PGDS in those with "late disease" versus "early disease" and teaches comparison of the levels of human L-PGDS in RA patients as compared to levels in normal patients and teaches comparison of human L-PGDS levels in patients with erosive versus non-erosive RA (i.e. determining the degree of dysfunction or severity) (see p. 11 lines 20-31, p. 12 and p. 85 lines 20 to 32).

Claims 1-10 are rejected under 35 U.S.C. 102(e) as being anticipated by Guild et al W) 2003/060465 published July 24, 2003.

Claim 1 and dependent claims are drawn to a method of detecting or differentiating rheumatoid arthritis, wherein the levels of human L-PGDS in a sample collected from a subject is measured.

Claim 3 and dependent claims are drawn to a method of determining the stage of disease with regard to rheumatoid arthritis, wherein the levels of human L-PGDS in a sample collected from a subject is measured and the stage of disease with regard to rheumatoid arthritis is estimated based on the measurement value.

Claim 5 and dependent claims are drawn to a method of determining the degree of dysfunction with regard to rheumatoid arthritis, wherein the levels of human L-PGDS in a sample is measured and the degree of dysfunction (severity) with regard to rheumatoid arthritis is estimated based on the measurement value.

As to claims 2, 4 and 6, the pre-determined cut-off values are not clearly set forth in the claims and therefore the cut-off values are interpreted as levels of human L-PGDS

in samples of healthy patients or in RA patients at different stage of disease or severity of disease.

Guild et al teaches a method of detecting rheumatoid arthritis (RA) wherein the levels of human L-PGDS in samples collected from a subject is measured. See abstract, p. 13 lines 17-21, p. 14 lines 6-22, p. 93 and table 1 and 2 p. 108 and p. 140 respectively, marker M177. Said samples include body fluids such as blood fluids, urine, synovial/joint fluid etc. See p. 4 lines 10-16. Said level of L-PGDS is measured by immunoassay. See p. 16 lines 32-34 and p. 16 lines 6-13. Guild et al also teaches determining the stage of rheumatoid arthritis ("late disease" versus "early disease") by comparing levels of L-PGDS in those with "late disease" versus "early disease" and teaches comparison of the levels of human L-PGDS in RA patients as compared to levels in normal patients and teaches comparison of human L-PGDS levels in patients with erosive versus non-erosive RA (i.e. determining the degree of dysfunction or severity) (see p. 11 lines 20-31, p. 12 and p. 85 lines 20 to 32).

Status of Claims

Claim 1-10 are rejected. No claims allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to OLUWATOSIN OGUNBIYI whose telephone number is 571-272-9939. The examiner can normally be reached on M-F 8:30 am- 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Oluwatosin Ogunbiyi/
Examiner, Art Unit 1645

/David J Blanchard/
Primary Examiner, Art Unit 1643